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10/568,364	02/14/2006	Lawrence J. Saubermann	BU-101XX	1148

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WEINGARTEN, SCHURGIN, GAGNEBIN & LEBOVICI LLP
TEN POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,364	SAUBERMANN ET AL.	
	Examiner	Art Unit	
	David A. Saunders	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS PENDING

Claims 1-14, filed on 2/14/06 are pending and are under examination.

OBJECTION(S) TO CLAIMS

Claim(s) 14 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The type of Th-1 associated condition, for which the kit is being used to diagnose/monitor, does not change the nature of what is provided in the kit as a chemical component - - e.g. interferon-gamma is interferon-gamma, whether it is being used to diagnose/monitor Crohn's disease, or SLE. The only kit component that might change, with the type of Th-1 associated condition, would be the instructions, which do not carry patentable weight.

REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the preamble recites "the level of immune activation and immunosuppression" while the conclusion recites "the level of immunologic activity and/or immunosuppression". A consistency in terminology and scope is required.

In claim 13, line 1, "The method" lacks antecedent basis.

REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant was not in possession of a method that can measure "the level of immune activation and immunosuppression in an individual" as recited in the preamble of claim 1. No individual can have both "immune activation and immunosuppression" at the time any one sample is collected. An individual with an imbalance in his immune system could have a state ot either one of "immune activation" or "immunosuppression", but not both simultaneously. Thus the preamble would properly recite - -the level of immune activation or immunosuppression- -. Likewise the conclusion would properly recite - -the level of immune activation or immunosuppression- -, rather than "the level of immunologic activity and/or immunosuppression".

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not given an adequate description of "a metabolic product of said pro-inflammatory substance".

Since all of metabolism is interconnected by multiple steps of conversion, activation, etc., one would not know how far removed from a "pro-inflammatory substance", such as a "chemotactic cytokine", its "metabolic product" might be. Any protein can metabolically breakdown to its constituent amino acids. Are amino acids among the "metabolic products"? One has no idea what the genus of "metabolic products" encompasses.

REJECTION(S) UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Romaschin et al (6,203,997, cited on PTO-1449).

Romaschin et al teach kits which provide an antigen as one of the chemical components. See col. 6, lines 21-33 and claim 12. The antigens contemplated by Romaschin et al include LPS, lipotechoic acid and TNF. See, for example, col. 1, lines 23-35; col. 2, lines 43-67; col. 6, lines 33-45; col. 10, lines 55-63 and claim 13. The TNF analyte/antigen contemplated by Romaschin et al would be TNF-alpha; see, for example col. 3, lines 29-33. These antigens contemplated by Romaschin et al are the same components as the "pro-inflammatory stimulant" provided in the instantly claimed kits. The open language of instant claim 10 permits the provision of other chemical components that are taught by Romaschin et al. Though the antigen components contemplated by Romaschin et al would be used in a different way and would be used to obtain a different diagnostic result from what is set forth in instant claim 10, the instant intended use does not preclude anticipation. Further, the provision of kit "instructions" in instant claim 10 does not preclude anticipation. See In re Ngai 70 USPQ2 1862.

Regarding claim 14, the instant intended use of the kit for diagnosing various recited autoimmune diseases does not preclude anticipation, because the type of Th-1 associated condition, for which the kit is being used to diagnose/monitor, does not change the nature of what is provided in the kit as a chemical component.

Claims 10 and 14 are rejected under 35 U.S.C. 102(b) or (e) as being anticipated by Rang et al (6,596,319, cited on PTO-1449 or US 2001/009680 A1, cited on PTO-892), in light of Tam (5,767,097, cited on PTO-892).

Rang et al (US 2001/009680 A1) and Rang et al (6,596,319) have 102 (b) and (e) dates, respectively.

Rang et al teach an immunomodulating composition which can be packaged in vials ('319 at col. 5, lines 62-63) or in sterile bottles ('319 at col. 21, lines 4-20). Such packaging is no different from the manner in which the "pro-inflammatory stimulant" could be provided in the instantly claimed kits.

Though Rang et al do not teach treatment/diagnosis of "Th-1associated conditions", their immunomodulating composition is properly considered to constitute a the "pro-inflammatory stimulant" of the Th-1 arm of the immune response. Note that the immunomodulating composition of Rang et al stimulates monocytes/macrophages to produce TNF-alpha. See '319 at, for example, col. 5, lines 44-46; col. 7, lines 48-59; col. 8, lines 1-6; col. 25, lines 40-57. TNF-alpha is taught by applicant as a "pro-inflammatory substance" that is released from WBC (e.g. spec. page 2). Tam (5,767,097) is cited as an evidentiary reference for teaching (col. 1, lines 10-27) that TNF–alpha is a Th1 cytokine. It is thus considered that Rang et al's immunomodulating composition constitutes a stimulant in accord with what applicant's contemplates as being a "pro-inflammatory stimulant". Thus Rang et al provide what applicant provides as a kit chemical component. A teaching of a chemical component corresponding to the "pro-inflammatory stimulant" is sufficient. There need be no teaching concerning the provision of kit "instructions", since "instructions" carry no patentable weight. See In re Ngai 70 USPQ2 1862.

Regarding claim 14, the instant intended use of the kit for diagnosing various recited autoimmune diseases does not preclude anticipation, according to the same rational set forth supra concerning Romaschin et al.

REJECTION(S) UNDER 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4 and 6-9 rejected under 35 U.S.C. 103(a) as being unpatentable over Marie et al, cited on PTO-892) in view of Levinson (6,066,322 cited on PTO-892).

Marie et al teach that whole blood samples, obtained from patients with sepsis, that are stimulated with LPS have a lowered production of TNF-alpha and IFN-gamma. See page 3439, col. 1. Applicant has taught that TNF-alpha and of IFN-gamma are associated with a Th-1 response. Applicant has taught that LPS indices a Th-1 response. Thus it is inherent that what Marie et al teach reflects a Th-1 response.

Marie et al do not teach how the TNF-alpha and of IFN-gamma were detected. They do, however detect secreted IL-8 is detected by an ELISA method; thus, at the least, it would have been obvious to use such a method in detecting secreted TNF-alpha and IFN-gamma, as reported at page 3439, col. 1.

Marie et al primarily focus on the mechanistic aspects that IL-8 might play in sepsis and do not specifically mention diagnosis. Levinson (6,066,322) teaches diagnostic and monitoring methods to determine whether a patient has a Th1 or a Th2 type response. He teaches that any variation in the expression of one or more nucleic acids or their encoded proteins may be used to diagnose/monitor shifts in the Th1 or Th2 type response. See cols. 55-61. Thus it would have been obvious that the shift in the production of TNF-alpha, of IFN-gamma, or of IL-8 that has been shown by Levinson would be used to diagnose/ monitor sepsis.

ART OF INTEREST

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Goodwin et al (5,569,585, cited on PTO-892) teach methods of determining the activation state of immune cells that have been stimulated with an intracellular acting stimulant, such as PMA or ionomycin. Such stimulants are known to increase the production of all cytokines, of both the Th1 and Th2 arms of the immune response. See Tam at col. 7, lines 6+ for such teaching.

Ochoa et al (5,658,744, cited on PTO-892) teach assessing immune status of patients by determining a ratio of a TH-1 type biological response modifier (BRM) to a Th-2 type BRM. The reference gives few details about how to do so. From what is disclosed (col. 22, lines 20-33), Ochoa et al show measurement of TH-1 type and Th-2 type lymphokines in serum, rather than in cultures of stimulated blood cells.

CONSIDERATION OF THE IDS

On Form PTO-1449, the Marie reference has been lined through because it was not fully cited. It has been cited on attached PTO-892.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 3/24/08 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644